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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/030,803

04/09/2002

Thomas Kissel

99/074 MED

5609

38263

7590

11/20/2006

EXAMINER

FUBARA, BLESSING M

PROPAT, L.L.C.

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CHARLOTTE, NC 28211-2841

ART UNIT

PAPER NUMBER

1618

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/030,803

Applicant(s)

KISSEL ET AL.

Examiner

Blessing M. Fubara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 August 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,6,8,10-15 and 19-24 is/are pending in the application.
- 4a) Of the above claim(s) 14 and 15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,6,8,10-13 and 19-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Examiner acknowledges receipt of request for extension of time, amendment and remarks filed 8/22/06. Claims 4, 5, 7, 9, 16 and 18 are canceled without prejudice. New claims 20-24 are added. Claims 1-3, 6, 8, 10-15 and 19-24 are pending. Claim 15 is withdrawn from consideration.

Response to Arguments

Previous rejections that are not reiterated herein are withdrawn.

Applicant traverses the withdrawal of claims 14 and 15 from consideration on the grounds that DNA and RNA are directed to methods associated with elected formula 1. Applicant was required to elect DNA or RNA or ribozyme in view of the burden of searching for claims 13-15. However, claims 14 and 15, which recite RNA and ribozyme, are withdrawn because of the burden to look for compositions/products containing DNA, RNA and ribozyme. The claim reciting DNA was searched and examined as was described in the previous action.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 1-3,6,8,10-13 and 19-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter,

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which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

The specification as filed does not provide support for “further comprising a moiety $[A]_w$.” Applicant points to page 6, lines 1 through 16 as providing support. However, the expression $[A]_w$ is not found.

The specification does not also provide support for $-O(CH_2)_pC(O)-$ with $p = 1$ and 3-10 basically excluding when $p = 2$. The specification at page 3 (amended sheet) provides support for $p = 1-10$ and 1 to 3 and not $p = 1$ and 3-10 or $p = 1$ and 3.

The specification does not also provide support for a compound where the hydrophilic non-ionic polymer is a 20-arm.

The specification does not provide support for 5000 to 10 000 000 g/mole. Support is however provided for 5000 to 50 000 and 100 to 10 000 000 g/mole. See replacement page 3, line 7.

The rejection above may be overcome by removing the new matter from the claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

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international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-3, 6 and 8 remain rejected under 35 U.S.C. 102(b) as being anticipated by Yokomichi et al. (US 5,204,196 cited by applicants on form PTO-1449). New claim 23 and 24 are included in this rejection. Therefore, claims 1-3, 6, 8, 23 and 24 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by Yokomichi et al. (US 5,204,196).

Yokomichi discloses PEG-X-PEI block copolymer (abstract; column 1, lines 34-46); PEG is the hydrophilic moiety having an average molecular weight of 550, which in the example 1 can go to a polymer having average polymerization degree of 11.8 and polyethyleneimine having average molecular weight of about 1300 and a polymerization degree of about 30 (Example 1). The molecular weight of PEI would be the degree of polymerization multiplied by the initial molecular weight of 1300, which would average to about 39000 to meet the limitations of the recited molecular weight for PEI. The molecular weight of the PEG would be the degree of polymerization multiplied by the initial molecular weight of 550, which would average to about 6490. Yokomichi discloses the copolymer of PEG and PEI. Furthermore, example 1 specifically adds sodium hydroxide to the solution of the PEI. The hydroxide ion meets the limitation of A- now recited in the claims. Surfactant in the context of claim 24 is a block copolymer of the nature disclosed by Yokomichi because as gleaned from the specification at page 11, lines 16 and 17, the block copolymers are surface active substances that are used as surfactants. Yokomichi thus meets the limitations of the claims.

Response to Arguments

6. Applicant's arguments filed 8/22/06 have been fully considered but they are not persuasive.

Applicant argues that the '196 patent, which is issued to Yokomichi recommends inclusion of straight chain PEI within its compositions, recommends using PEO "having a maximum degree of polymerization of 100 (i.e. a molecular weight of 4400)" in a conduction polymer because PEO of higher molecular weight is "detrimental to ionic conductivity." Therefore, applicant argues that modifying the '196 patent by using PEO having a molecular weight of 5000 would render the conductive polymer unfit for the intended purpose. Applicant further argues that the '196 patent does not suggest beneficial effect of using cyclic, star, dendritic, 4-arm, 8-arm or 20-arm branched polyethylene glycol of claims 20 and 21.

Response:

Examiner agrees with applicant that straight chain PEI is suggested for use in the product of the '196 patent and applicant's attention is drawn to instant claims 1-3 where "linear" PEI is one of the choices for the PEI in that compound. Therefore, straight chain PEI meets the limitation of claims 1-3. The '196 patent does say in column 2, lines 1-3, that PEO having "more than 100 of polymerization degree" results in film that has good shape but "undermined" conductivity. The '196 patent does not state the molecular weight at 4400 for the PEO/PEG. Specifically, polymerization degree or degree of polymerization DP is

$$DP = \frac{M_t}{M_0}$$

where M_t = molecular weight at time t and M_0 = molecular weight of one monomeric unit.

The monomeric unit of PEO in Example 1 has a molecular weight of 550 and a DP of 100 would mean that the average molecular weight of the PEO polymer would be 55000. However, the DP in Example 1 is disclosed to be 11.8, which will mean that the molecular weight of the PEO/PEG would be 6490. In both cases, the molecular weight of the PEO/PEG meets the limitation of 5000 to 10 000 000 since 55000 or 6490 would touch a point within the recited range. It appears that the '196 patent would mean that the molecular weight of the PEO should not exceed 55000 in order to not undermine the conductivity of the polymer if the initial weight of the PEO/PEG is 550. It is also note worthy that the '196 patent, in that text referred to by the applicant, does not particularly disclose the initial molecular weight of the PEO/PEG. Cyclic, star, dendritic, 4-arm, 8-arm or 20-arm branched polyethylene glycol of claims 20 and 21 are not limitations in claims 1-3.

7. Claims 1-3, 6, 8, 10-13 and 19 remain rejected and new claim 24 is rejected under 35 U.S.C. 102(a) as being anticipated by WO 98/59064, cited by applicants on form PTO-1449 and the specification which is the same as US 2001/0005717 to Wagner as pointed out by applicant. Therefore, Claims 1-3, 6, 8, 10-13 and 19 and new claim 24 are rejected under 35 U.S.C. 102(e) as being anticipated Wagner et al. (US 2001/0005717).

WO 98/59064 discloses DNA complexes with PEG-PEI conjugate copolymer (English abstract; Examples 1-3), methoxy-succinimidyl propionate PEG (M-SPA-PEG) reacts with the

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imine (Example 2); the molecular weights of the PEG and PEI meet the limitations of the recited molecular weight (Example 2). The DNA is contacted with the complex of PEG and PEI (Examples 1 and 2). The WO publication and the English equivalent of the WO publication meet the limits of the claims. Methoxy-succinimidyl propionate (Example 2) is anionic and complex union with PEG stabilizes PEI. Water, which provides hydroxyl groups, which could also meet the limitation of anion. Surfactant in the context of claim 24 is a block copolymer of the nature disclosed by Wagner because as gleaned from the specification at page 11, lines 16 and 17, the block copolymers are surface-active substances that are used as surfactants.

Response to Arguments

8. Applicant's arguments filed 8/22/06 have been fully considered but they are not persuasive.

Applicant's argument is based on the US publication 2001/0005717 A1, which is the English equivalent of the WO reference.

Applicant contends that PEI imparts increased tendency for aggregation, which is evidenced by the state of the art in paragraphs [0003], [0012] and [0023] of the published application in English. Applicant states that the combination of non-ionic polymer and neutralizing anion masks the positive charge of the PEI and that the claimed invention includes a cationic core of PEI and a hydrophilic shell of PEO, which is obtained by using a 3- to 10- or 25-fold excess of PEI as can be seen according to applicant in page 9, line 10 of the as filed specification.

Response:

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In referring back to the specification, applicant is attempting to export limitation from the specification into the claims and although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims do not recite a core structure and thus the prior art does not have to teach a core structure to meet the claims. Paragraph [0003] of Wagner discloses that a size of not more than 200 nm allows uptake of complexes into the coated pits. Paragraph [0012] of Wagner, discloses that the mobility of the polymer chain appear to be responsible for the protective effect of PEG and longer half lives of liposomes. Further, paragraph [0023] discloses that the hydrophilic polymer bound to PEI is preferably linear or branched to a small extent to ensure that mobility is maintained. In this regard, examiner finds no contradictory teaching as it relates to claims 1-3, 6, 8, 10-13 and 19 because the claims are directed to linear or branched A and linear or branched B. The linear nature of the polymer in the prior art meets the limitation of linear in these claims. The claims are not directed to method of making the polymer/compound but to a compound that comprises A, B and X so that the use of 3- to 10- or 25-fold excess of PEI is not reflected in the claims and do not constitute limitation in the instant claims. The methoxy-succinimydyl propionate serves as the anionic component.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 10-13 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yokomichi et al. (US 5,204,196 cited by applicants on form PTO-1449) in view of Ogris et al. ("PEGylated DNA/transferrin-PEI-complexes: reduced interaction with blood components, extended circulation in blood and potential for systemic gene delivery" in **Gene Therapy** Volume 6, Issue 4 , April 1999, Pages 595-605).

12. Yokomichi discloses PEG-X-PEI block copolymer (abstract; column 1, lines 34-46); PEG is the hydrophilic moiety having an average molecular weight of 550, which in the example 1 can go to a polymer having average polymerization degree of 11.8 and polyethyleneimine having average molecular weight of about 1300 and a polymerization degree of about 30 (Example 1). The molecular weight of PEI would be the degree of polymerization multiplied by the initial molecular weight of 1300, which would average to about 39000 to meet the limitations of the recited molecular weight for PEI. The molecular weight of the PEG would be the degree of polymerization multiplied by the initial molecular weight of 550, which would average to about 6490. Yokomichi discloses the copolymer of PEG and PEI. Furthermore, example 1

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specifically adds sodium hydroxide to the solution of the PEI. The hydroxide ion meets the limitation of A- now recited in the claims. Yokomichi does not disclose a complex of DNA with the copolymer. However, Ogris discloses that the complexes can be formed between DNA and PEI and PEG and the complex is formed by contacting the DNA with PEI and PEG (abstract). According to Ogris, pegylation of the complexes reduces plasma protein binding and erythrocyte aggregation, the pegylated complex mediated reporter gene transfer to tumor without significant toxicity. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare pegylated DNA complex with PEI with the expectation that therapy with the pegylated DNA complex would reduce toxicity while reducing protein binding and erythrocyte aggregation.

Response to Arguments

13. Applicant's arguments filed 8/22/06 have been fully considered but they are not persuasive.

Applicant argues that the Gene Therapy reference does not cure the deficiencies of the US '196, that Gene Therapy is broadly directed to DNA/transferring-polyethyleneimine complexes which have been "pegylated" to reduce plasma protein binding and erythrocyte aggregation, that Gene Therapy does not teach or suggest complexes which include non-ionic polymer with the recited molecular weight of from 5000 to 10 000 000 g/mole and does not disclose advantages of combining non-ionic polymers with PEI, that Gene Therapy does not teach or suggest cyclic, star, dendritic, 4-arm, 8-arm or 20-arm branched polyethylene glycol of claims 20 and 21. That Gene Therapy cannot be combined with the '196 patent because they

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are in different fields of endeavor and that the combination would not result in a complex that includes neutralized PEI, non-ionic polymer having molecular weight of from 5000 to 10 000 000 g/mole, and PEO/PEG that is cyclic, star, dendritic, branched 4-arm, 8-arm or 20-arm.

Response:

The rejected claims recite linear or branched and the primary art “196 disclosing linear PEG or PEI meet the limitation of linear in the rejected claims. Therefore, the combination does not have to teach PEO/PEG that is cyclic, star, dendritic, branched 4-arm, 8-arm or 20-arm. The molecular weight of PEO/PEG is expected at 6490 or 55000 depending on degree of polymerization of 11.8 or 100 and as such, the molecular weight requirement of the amended claims is met by the ‘196 patent. Since applicant assumes that the ‘196 patent is deficient in the molecular weight of the hydrophilic polymer now required, and since it has been shown that the ‘196 patent is not deficient in molecular weight since the projected molecular weight may lie between 6490 and 55000 depending on the degree of polymerization, the Gene Therapy reference does not have to cure that deficiency. Regarding applicant’s argument that a conductive polymer such as that disclosed in the ‘196 patent cannot be combined with a DNA/transferring containing polyethyleneimine complex, it has been held that a prior art reference must either be in the field of applicant’s endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the conductive polymer of the ‘196 patent is broadly viewed as a polymer that is able to conduct or move associated molecules of ions in solution such that association of the conductive polymer with the DNA/transferring-PEI complex

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would lead conducting or movement or delivering of any ions/DNA associated with the over all complex. When applicant separately considers individual references in a discussion where two references are combined to explain the obviousness of a claimed invention over the prior art, applicant is arguing against the references individually. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

No claim is allowed.

14. This application contains claims 14 and 15 drawn to an invention nonelected with traverse in Paper No. 11/29/05. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594.

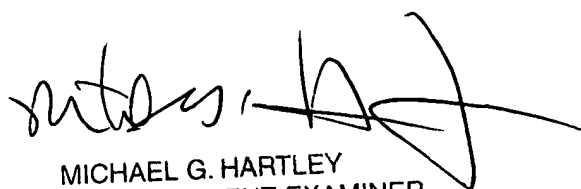
The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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